

Appl. No. 09/431,607
Amdt. dated November 1, 2005
Response to Notice of Allowance September 19, 2005

PATENT

Amendments to the Drawings:

The attached sheets of formal drawings include minor corrections to Figs. 1, 2, 4, 5, 6, 7, 10, 13, and 14. These drawings replace the original sheets of informal drawings.

Attachment: Replacement Sheets
Annotated Sheets Showing Changes

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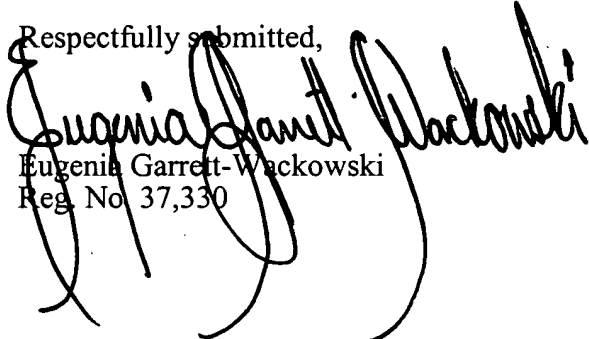
REMARKS/ARGUMENTS

The Examiner accepted the drawings which were filed on November 1, 1999.
Upon further review of the drawings, Applicant discovered that the drawings were informal.
Applicants request that the replacement drawings be printed in the patent to issue.

CONCLUSION

Entry of this amendment is respectfully urged since it does not touch the merits.

Respectfully submitted,


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Attachments
EGW:lls
60624868 v1

Figure 1

Conservation of CCHC Type Retroviral Zinc Fingers
 (-Cys-(X)2-Cys-(X)4-His-(X)4-Cys-)
 Among Known Retroviruses

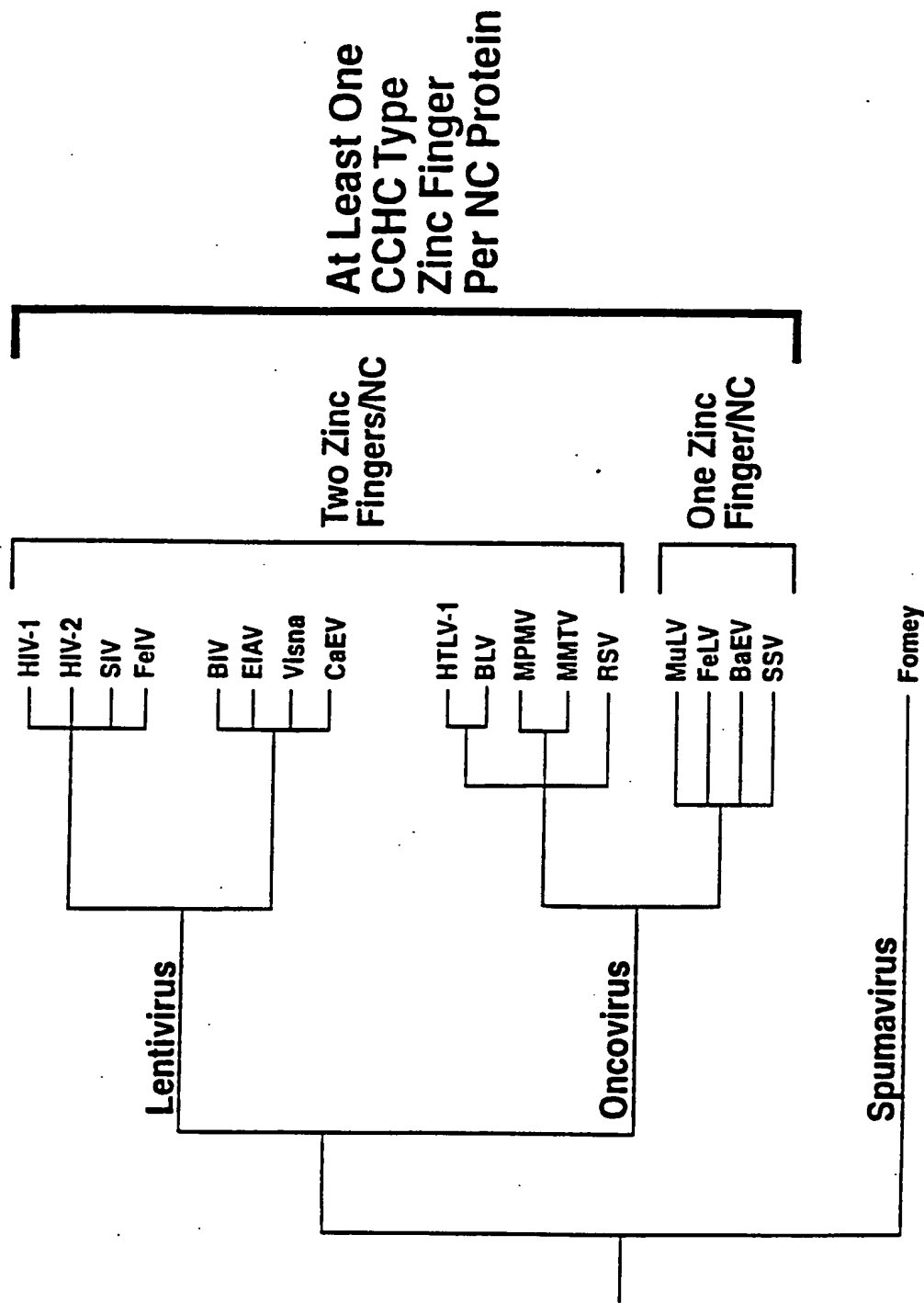
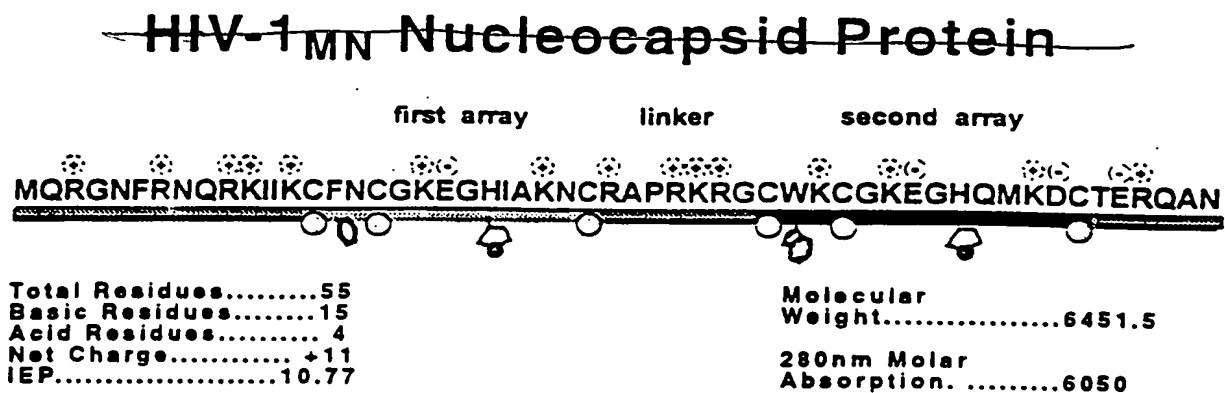
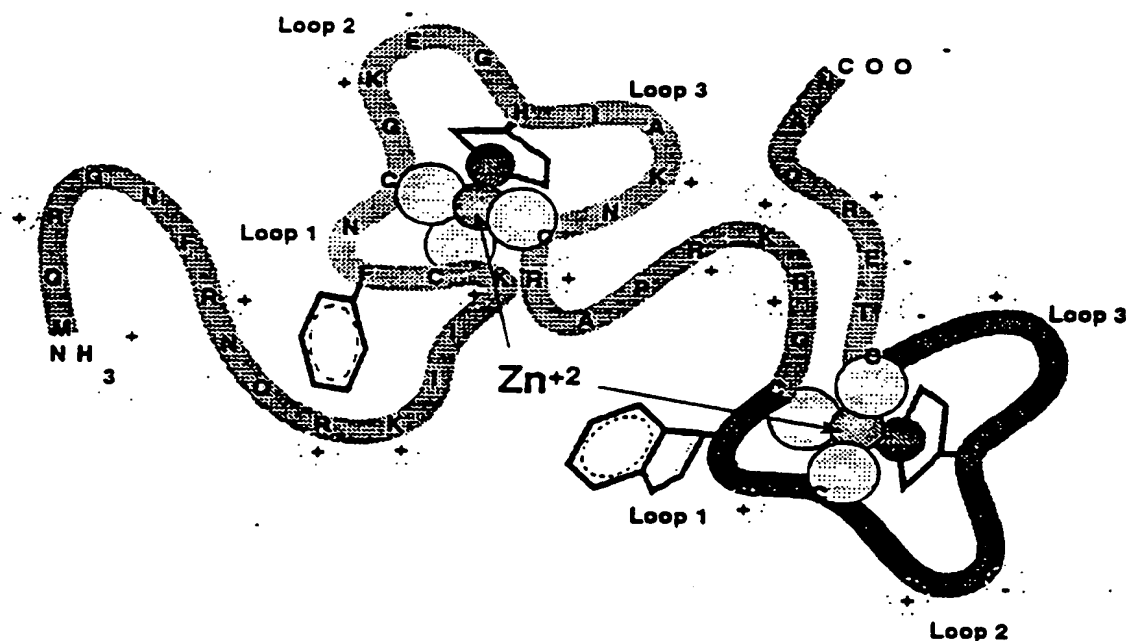


Figure 2



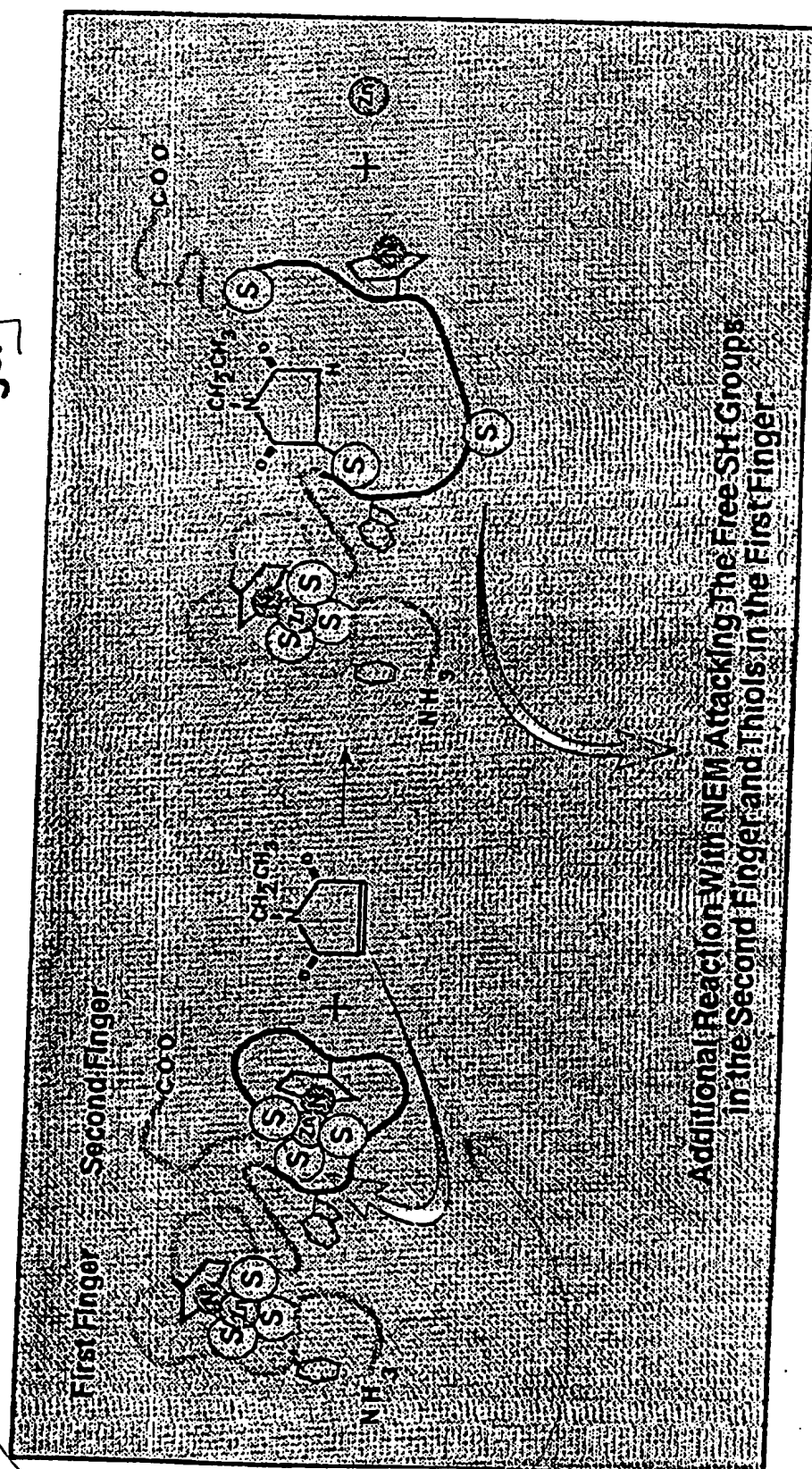
First Zinc Finger



Second Zinc Finger

Figure 4

The Initial Reaction With NEM Modifies The First Cys Residue In The Second Finger



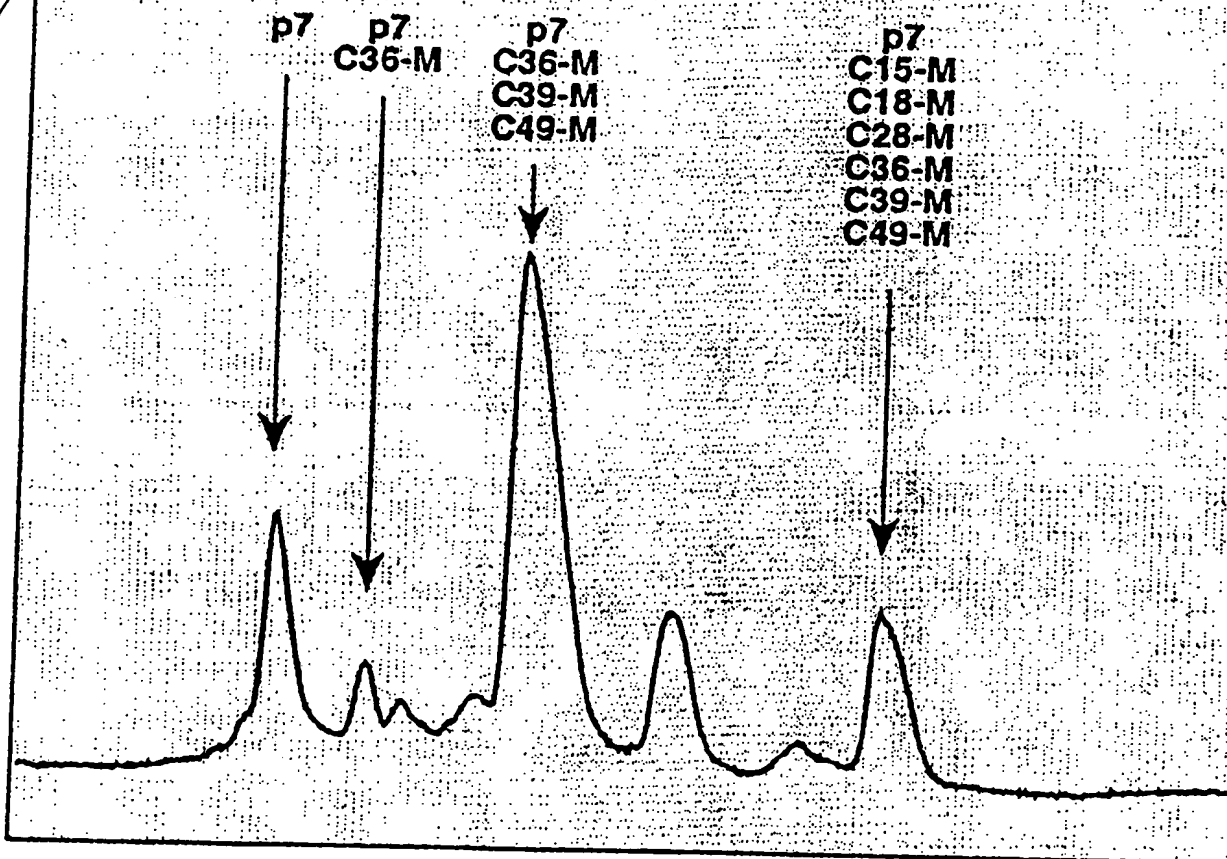
Additional Reaction With NEM Attacking The Free SH Groups In The Second Finger and Thiols In The First Finger

By reacting p7NC with limiting amounts of NEM and analyzing as in Fig. 6, it was determined that the first cysteine in the second zinc finger reacts fastest with the reagent. This is an example showing how the procedures have been used to investigate the reaction pathway and to determine the most reactive thiol in the NC protein.

FIGURE 5

Analysis of Reaction Products by HPLC

The positions of alkylated Cys residues were determined by sequence analysis of separated proteins and are indicated by the notation C#-M.



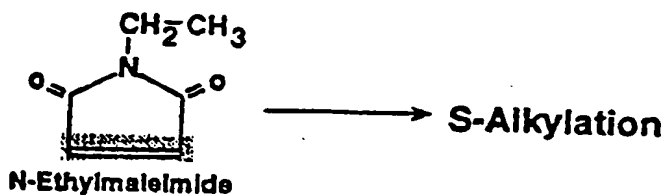
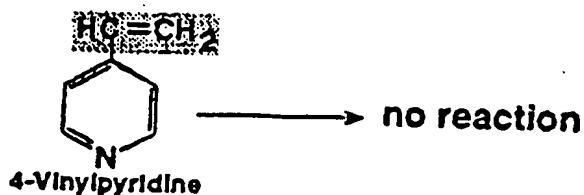
Reaction conditions: 62 mM p7NC + 744 mM NEM; pH 7.0, 60min. at RT.

Separation was accomplished by reversed phase HPLC using a C-18 μ -Bondapak (3.9 x 300 mm) column (Waters, Inc). Proteins were eluted at a flow rate of 1.0 ml/min. with gradients of acetonitrile (0-17, 20 min. 17-25, 120 min.) at pH 2.0 (0.05% trifluoroacetic acid). Proteins were detected by UV absorption at 206 nm.

FIGURE 6

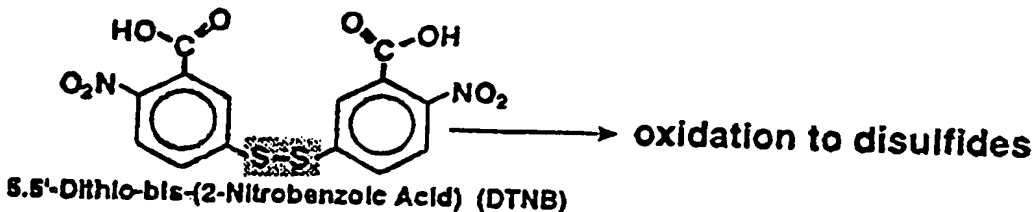
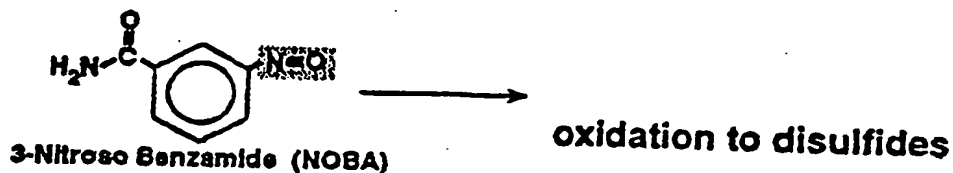
~~REACTIONS OF HIV-1 NC~~ ~~RETROVIRAL CCHC ZINC FINGERS~~

Reagent Reaction With p7NC



Cu^{+2} → oxidation to disulfides

Fe^{+3} → oxidation to disulfides



Glutathione


 Glutathione

→ no reaction

The reactive functional groups are shaded

Figure 7

~~Functional Groups Which React With Retroviral Zinc Fingers~~

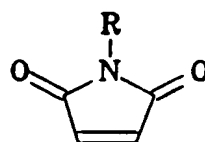
disulfides



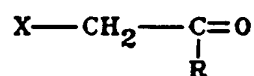
nitroso compounds



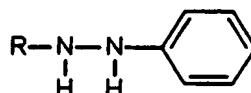
maleimides



α -halogenated ketones



phenylhydrazids



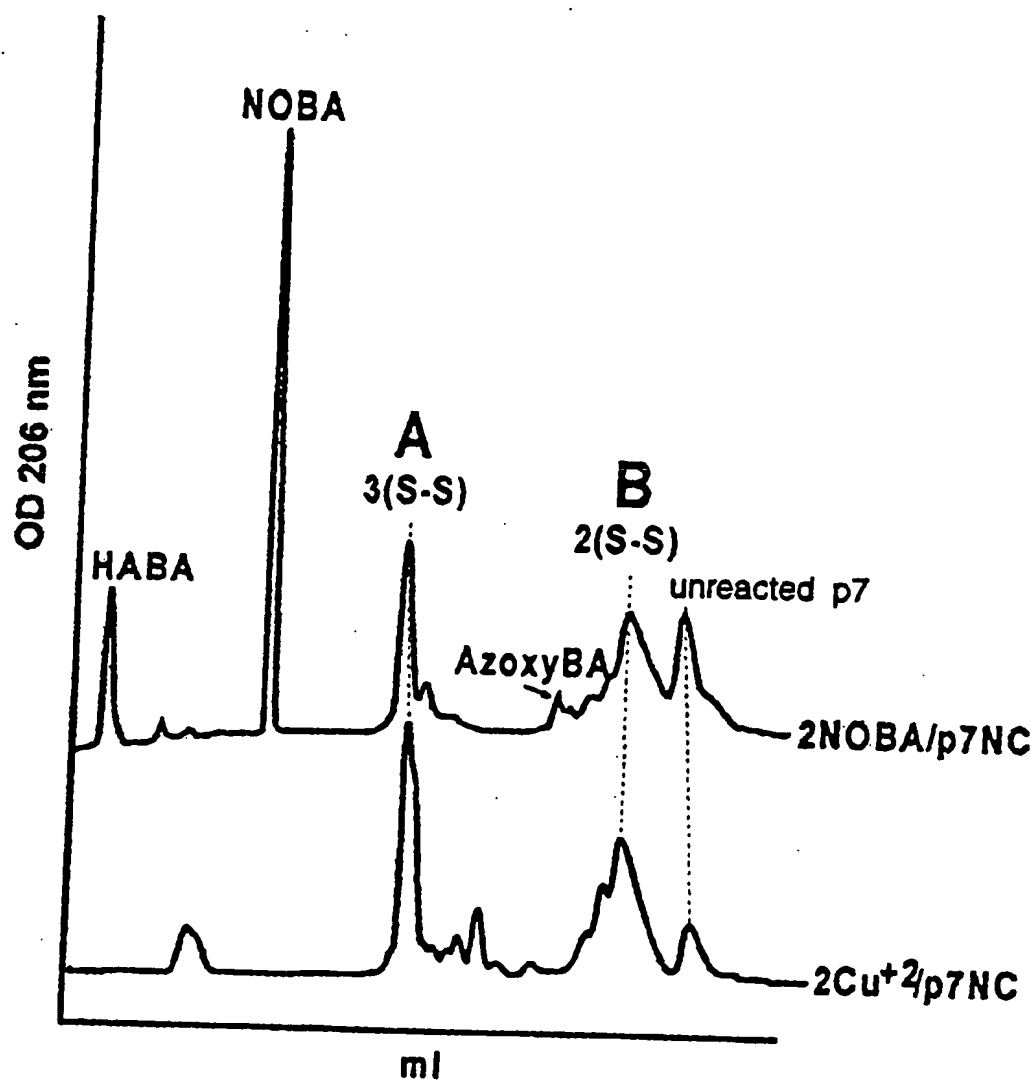
Nitric Oxide and Derivitives NO

cupric ions and complexes Cu^{+2}

ferric ions and complexes Fe^{+3}

wherein R is any atom or molecule, and X is selected from the group consisting of F, I, Br and Cl.

FIGURE 10



~~HPLC Chromatograms of NOBA and Cupric~~
~~Oxidation Products of p7NC~~

FIGURE 13

~~HPLC Analysis Of p7NC Reactions With~~ ~~Imuthiol and Disulfiram~~

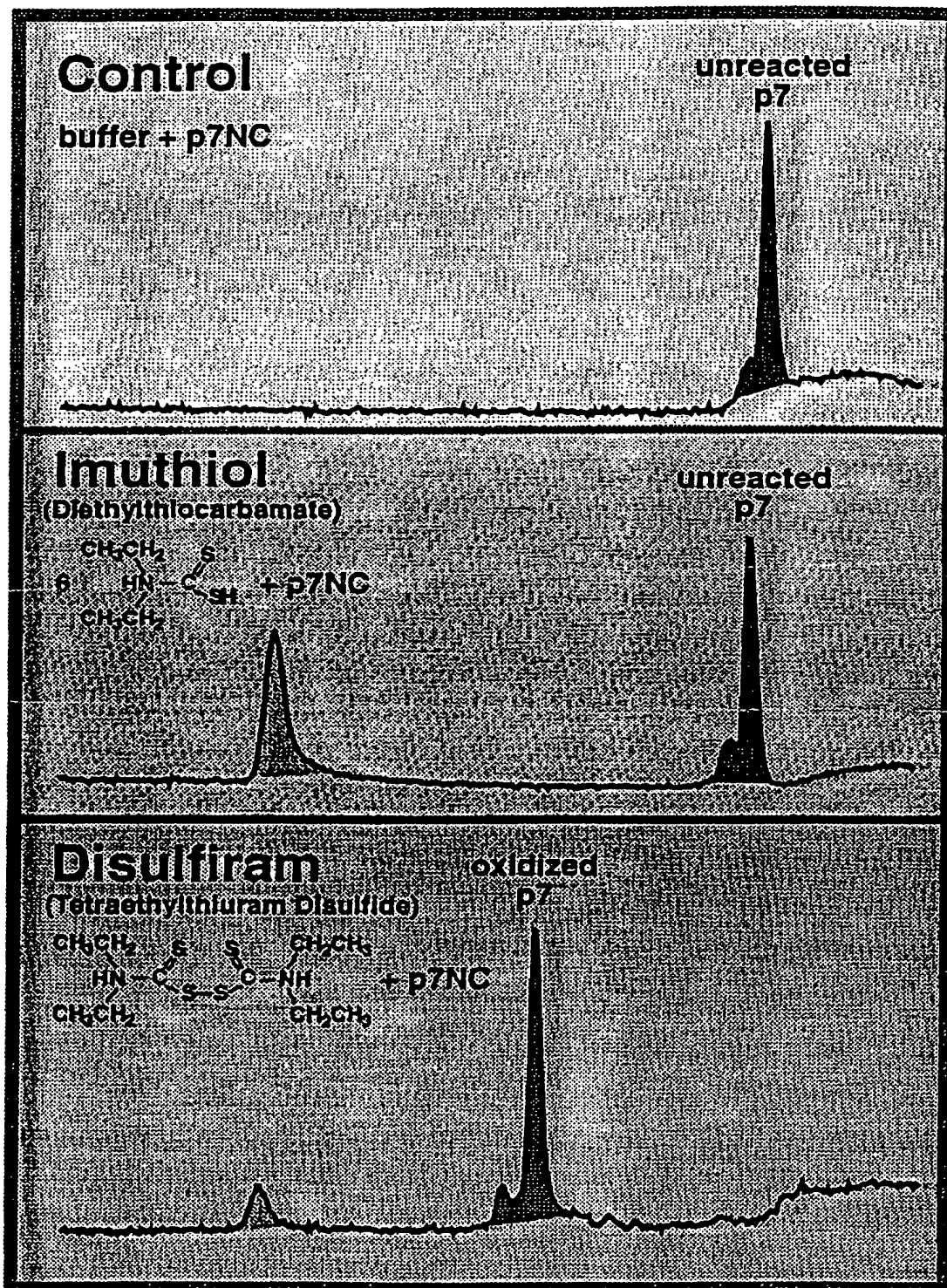
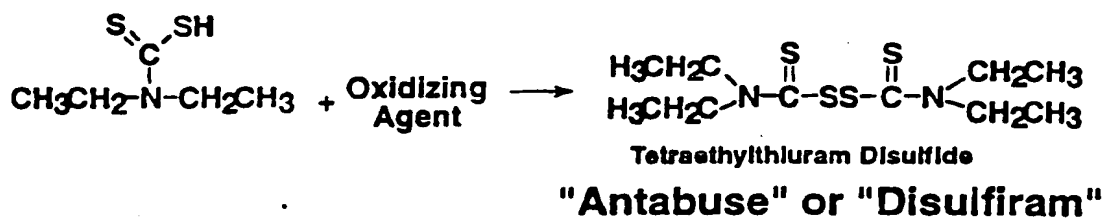
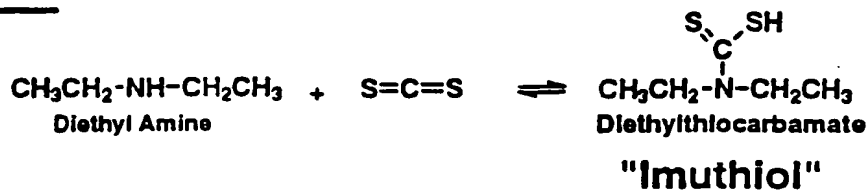


FIGURE 14

~~Medical Use and Chemistry of Thiurams~~

Synthesis



General Reactions

